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On Arterial Tonicity

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On Arterial Tonicity.

Arterial Tonicity is of two kinds according as its existence depends upon central or upon peripheral influences. Notwithstanding the protests of Goltz, physiologists now generally agree in regarding the dilatation of an artery, which follows the cutting of its nerve, as the direct result of the removal of constrictive agencies, which

have "their origin in the vasomotor centres & continuously descend along the nerves to the muscular arterial coats. This dilation, first observed by Pourfour du Petit in 1727 was not extensively studied until 1851, when began the active work of Bernard, Brown Sequard, Schiff, & others upon the question of the existence & nature of vasomotor nerves.

By observing the general dilation of the vessels following upon the destruction of a portion of the medulla at the calamus scriptorius, Schiff in 1855 first located the vasomotor centre in that region. Nine years later Goltz found evidence of the

separate existence in the spinal cord of definitely localized areas possessed of a vasomotor governing function. But the continuous activity of medullary and cord centres was an hypothesis insufficient to account for all the phenomena, since it was observed that the dilation of an artery, caused by severance from those centres, gave way after a few days to a permanent constriction, subject, however, as before to temporary variations in degree. Indeed in some cases, as with the nerves supplying the submaxillary gland, section did not produce dilation. The existence of a local tone the intrinsic property of the vessels themselves, could not hence be denied, and [illegible]

cause of the maintenance of such a tone has since been sought in various directions.

It was Bidder, who in 1866 first ascribed to peripheral ganglia the power of causing arterial constriction; & in 1874 Goltz began the publication of his well-known series of papers, endeavoring to establish the paramount importance of the peripheral mechanism whether ganglionic or muscular in nature. The hypothetical peripheral ganglia have not been found & many physiologists claim with Bernstein that it is most reasonable to suppose the vascular tone to originate in the arterial muscle cells themselves. Yet, if we accept this view, we must

still look for a cause for the contraction of the muscle cells & for the variations in the amount of such contraction which are known to take place normally in the body.

Up to the present time, but one theory has been advanced to explain all these phenomena — the theory proposed by Gaskell in 1880.

Gaskell found that the addition of a small quantity of a solution of sodic hydrate to a neutral fluid circulating through the arteries of a frog was followed by a constriction of the vessels to a degree varying with the amount of the drug present. He further found that lactic acid introduced

into the neutral circulating fluid acted in an opposite manner, putting the arteries into extreme dilatation. Moreover the constriction brought about by sodic hydrate was with acid quickly replaced by dilatation; and the dilatation produced by lactic acid was with sodic hydrate quickly replaced by constriction. From these facts Gaskell drew the general conclusion that alkalies cause constriction & acids cause dilatation of the arteries; and he proposed to account for the ever present arterial tonicity by supposing the alkalinity of the juices bathing the walls of the arteries to exert its constricting action upon the muscle cells. The production of an acid by tissue activity

as, e.g. the contraction of a muscle, would diminish the alkalinity of the fluids & hence diminish arterial tonicity. Variations in the latter would thus be explained by variations in the degree of alkalinity of the surrounding fluids. Gaskell extended his theory to the explanation of cardiac tonicity, since sodic hydrate and lactic acid were found to have upon the heart effects similar to those exerted upon the arteries, i.e. the former brought about a standstill of the heart in systole, the latter a standstill in diastole.

The forming of so radical a theory upon such apparently insufficient experimental grounds, for the author has employed in his

work but one alkali + that not one which is present in the body, was noticed by Ringer & Buxton (2) and they were led to investigate the question more fully by experiment. They studied the heart only, obtaining with sodic hydrate the same results which Gaskell had obtained. Turning then to the normal alkalies of the blood, they found that sodic bicarbonate gave a similar stoppage of the heart in systole. With sodic phosphate alone, "a possible source of alkalinity other than the bicarbonate" of the blood, but little increase in cardiac tonicity was observed. But they found further that potassium chloride, also a normal constituent of the blood, when introduced into the neutral circulating

fuse, either quite removed, to use the acid putting the heart into a state of extreme relaxation; after the production of a systolic condition by soda hydrate or soda bicarbonate; the addition of a small quantity of potassium chloride completely counteracted the effect of the alkali, the tonicity of the heart muscles giving place to relaxation". They did not extend their researches to the arteries but Ringer & Sainsbury (3) had previously shown that soda bicarbonate by itself causes arterial constriction, yet this constriction does not appear in the presence of potassium chloride

Ringer & Buxton hence claimed that neither cardiac nor arterial tonicity can be explained as due to the direct action of alkaline fluid upon the muscle cells, since the constant presence of the potassium chloride will prevent the sodic bicarbonate from exerting its characteristic action.

The antagonism of the views of Gaskell & of Ringer & Buxton and the lack in the latter's work of experimental evidence as to the arteries, has induced me to test for these vessels the validity of the objections to Gaskell's theory.

My method of work has been the same as that employed by Stevens & myself (41) in determining the

action of fibrin ferment upon the arteries & is described in full in our paper upon that subject. In all of my experiments terrapins were employed and the brain & spinal cord were completely destroyed at the beginning of the operation. The anterior part of the plastron was then removed, exposing the heart & great vessels; the heart was cut out & inflow cannulas were inserted into the left systemic aorta & into the bulbus arteriosus just before the right systemic aorta was given off; the pulmonary arteries were ligated, together with all arteries supplying the head & fore-legs, since the rupture of the vessels by the distention of

the brain & spinal cord would not have allowed a circulation through those parts; a pressure cannula was inserted into the stump of the right brachial artery, a large outflow cannula was placed upright in the sinus venosus and the animal was then ready for the experiment. The circulating fluid was a 0.75 % solution of NaCl in distilled water, & was supplied from a Mariotte's flask. Between the flask & the animal's body was placed the artificial heart described by Stevens & myself, the function of the instrument being to force the circulating fluid coming from the flask into the arteries of the animal in an in-

termittent stream. The venous pressure of the heart i.e. the height of the lower end of the inflow air tube of the Mariotte's flask above the heart was 14 cm and the animal was placed on a level with the heart. Circulation was thus possible thro the hind limbs & abdominal viscera, the circulating liquid returning to the venous sinus was caught, as it came through the outflow tube, and measured. Arterial pressure was registered upon a revolving drum. The drug, the action of which was to be tested, was dissolved in normal salt solution & supplied to the arteries from a second flask standing [illegible]

the one containing the neutral circulating fluid. I have investigated the actions of sodic hydrate, sodic bicarbonate, sodic phosphate, lactic acid & potassium chloride. The sodic bicarbonate was manufactured by Merck of Darmstadt. The sodic phosphate was of the same manufacture & was purified & recrystallized by myself. The potassium chloride was supplied by Eimer & Amend of New York & was also carefully recrystallized to exclude all possibility of the presence of impurity.

1. I found sodic hydrate to be the most powerful of all the drugs used as regards the constriction of the arteries, a solution of strength

1-20000, i.e. 1 part drug to 20000 parts
salt solution; causing a rapid dimin-
ution in the outflow accompanied by
a great rise of arterial pressure.
2. Solutions of sodic bicarbonate (1-2500)
caused constriction & stronger solutions
produced much more marked effect
upon the pressure & outflow.
3. Solutions of sodic phosphate
(1-500) gave slight constriction; solu-
tions of strength (1-250) narrowed the
arteries very considerably — in one
case diminishing the outflow from
30.4 cc. to 5.2 c.c & increasing the
pressure from 18 mm. Hg. to 24 m.m
These results with sodic phosphate
are quite opposed to those obtain-
-ed from the heart by Ringer &
Buxton; & it is hardly reasonable
to suppose the difference to be due

to any difference in concentration between the heart & the arteries. My experiments with sodic phosphate have been numerous & in no case has it failed to produce constriction.

4. Lactic acid in proportion (1-10000) gave dilation. Contrary to the testimony of Gaskell, this dilation could be recovered from by normal salt solution alone.

5. Potassium chloride (1-10000) produced, as Ringer & Buxton claim, dilation; the action being distinct & unmistakable, though in some cases not persisting long even when KCl was kept circulating. The action of potassium chloride seems however to be somewhat exaggerated by Ringer & Buxton, for I have found that di-

cation produced by a comparatively strong solution of KCl (1-2000) is at once set aside + constriction brought about by the addition of $NaHCO_3$ in proportion, 1-1000.

Ringer + Buxton lay great stress upon the simple fact that a condition of increased tonicity produced by a drug, as e.g. sodic bicarbonate, may be replaced by an atonic state upon the addition to the circulating fluid of a sufficient quantity of potassium chloride – a proposition which no one can deny. But to conclude from this, as they do, that the alkaline salts of the blood do not maintain arterial tonicity is unjustifiable. In reference in our experiments

"the physiological conditions which are present in the blood", as they desire to do, it is necessary to introduce into our circulating liquid at the same time both $NaHCO_3$ & KCl and these in proportions such as exist in the blood itself. So far as it appears from the paper of Ringer & Buxton, they have not done this. In attempting it, we are, of course, at once hampered by the fact that absolute knowledge regarding the salts of the plasma is so far wanting. In my experiments touching this point I have relied upon the best known & most widely accepted analyses of the blood. The blood of the terrapin has, I beleive, never been

completely analysed of mammalian blood, the analyses of Schmidt + of Sertoli are probably the most reliable. According to Schmidt, plasma contains of Na_2O 0.1532%, which, computed as sodic bicarbonate, its probable compound in the blood, equals 0.2075%. Sertoli gives of Na_2O 0.116% in serum, equivalent to 0.157% of $NaHCO_3$. The latter does not mention potassium chloride in his table + hence I have employed with each proportion of $NaHCO_3$ the proportion of KCl given by Schmidt, viz:- 0.0359%. The following results taken from Experiment 35, April 2, 1885 are typical as showing the effect of a mixture of $NaHCO_3$ + KCl accord-

ing to Schmidt's analysis.

Time P.M.	Temp. surrounding animal C	Arterial Pressure mm Hg	Venous Outflow per minute cc	Remarks
3.21	21.5°	22 7	1.5	.75% NaCl solution circulating.
24		21 7	1.7	
27		21 1	1.7	On $NaHCO_3$ .2075% (Schmidt) + KCl
.30		21 8	2.1	.0359% (Schmidt) in .75% NaCl solution
.33		21 4	2.4	
36		21.5	2.4	
39		23	1.9	
42		23.5	1.5	
45		[illegible]1	1.3	
48		26.4	1.6	
51		21 1	1.3	
54		25 7	1.4	
57		30.5	1.2	
4.00		25.7	1.5	Off $NaHCO_3$ + KCl.

4.03		30.5	1 4	
.06		33 7	1 2	
09		27.6	1.3	
12		37.5	1 4	
15		35.8	0.8	
18		32 8	0.7	
21		31.7	1.	
24		28 4	1.1	
.27		25 4	1.5	
30		24 7	1.3	
.33		23	1.3	
36		22.8	1 7	
39		21.7	2.1	
42		21 5	1.1	
48		22.3	1.8	
45		21.7	1.7	
51		21.7	1 7	In $NaHCO_3$ + KCl in same propor-
54		22.0	1 8	tion as above.
.57		21.7	1.7	

.500	21.3	21.1	19	
03		21.7	18	
06		23.8	16	
09		24.4	1.4	
12		25.4	1 [illegible]	Off $NaHCO_3$ + HCl
15		25.8	15	
18		25.9	1.7	
.21		29.5	1.4	
.24		33.5	1.4	
.27	21.3	30.2	1.1	Experiment ended

We see here that the ultimate effect of the mixture of $NaHCO_3$ + HCl is in all cases constriction of the arteries manifested by a rise of pressure and a decrease in outflow. The constriction is slow to appear, i.e. is after [illegible]

is a slight dilatation, as if the KCl first affected the muscle cells but was overcome by the more slowly acting $NaHCO_3$. The table illustrates one other phenomenon frequently met with, i.e. the great difficulty experienced in bringing back the vessels to their former condition by the use of salt solution. After the alkaline solution is turned off, the constriction usually rises to a still higher degree & the pulse curve often becomes irregular, now rising, now falling. This continues for some minutes, but the normal salt solution gradually forces its way into the vessels & washes out the alkali, & the vessels finally succumb & return to their former

dilation. The mixture of sodic bicarbonate 0.157% (Sertoli) and potassium chloride 0.0359% (Schmidt) also gives constriction, although here the sodic bicarbonate is in much smaller proportion than according to Schmidt's analysis.

From the results of my experiments upon the effects of sodic bicarbonate, sodic phosphate, + potassium chloride, it would then appear that the quantity of potassium chloride normally present in the blood is insufficient to prevent the constricting action of the alkaline salts upon the arteries at least, such action is due primarily to the sodic bicarbonate yet the tendency of the sodic phosphate is in the

same direction. But the effect of these two salts alone in the proportions in which they exist in the blood would be enormous + a serious hindrance to circulation. The slight dilating action of the KCl would hence seem necessary to modify + tone down the constriction + its presence in the blood would rather argue for than against the theory of the maintenance of arteriae tonicity by the alkaline salts. The difficulty experienced in recovering after a circulation of the sodic bicarbonate + potassic chloride favors the same theory + recalls a phenomenon often witnessed at the beginning of a circulation experiment. When the salt sol-

ution is being first admitted to the vessels & the animal's blood is being washed out, it is not rare to have great irregularities in the pulse curve with an exceedingly high average blood pressure. As the experiments proceeds the pressure falls to a lower level & remains uniform.

The probable constancy of the proportion of potassium chloride in the blood obliges us to look elsewhere for the cause of variations in arterial tonicity. The fact that, as Gaskell points out, the activity of a tissue results in the production of an acid & the known fact that in muscle work the alkalinity of the blood is diminished by the formation

of acid point with great probability to the correctness of the view that acids so produced are the active agents in the diminution of local tonicity.

I now come to the consideration of another theory as to the cause of arterial tonicity, which was first suggested last year by Stevens & myself (4). It is a well known fact that the smooth muscle of the intestine is very sensitive to mechanical stimuli - drawing a needle across the surface of the intestine will cause a slowly appearing but often very considerable contraction of both the longitudinal & the circu-

far muscular layers. A similar phenomenon may be seen in an artery similarly stimulated. I have many times observed it in the terrapin. Slightly pinching the vessel with a small pair of forceps, pressing it with the side of a needle, or giving it a slight blow will produce a decided contraction at the place of stimulation. This appears in four or five seconds after the stimulus has been applied slowly & gradually increases, reaches its maximum, where it remains for a short time, & then as slowly & gradually gives place to relaxation, the whole cycle of changes sometimes requiring more than a minute. I have observed an artery

of half a millimetre in diameter thus gradually to constrict to about one half its former size upon a slight pinch being given it by a pair of forceps. Such a contraction differs from that occurring in the intestinal wall in that it is not peristaltic – it exists only at the point of stimulation & does not travel away from that point. This fact seems peculiar when we consider how readily in the intestine the circular contraction is transmitted in a longitudinal direction. Nevertheless in numerous observations made upon arteries of various sizes, & where the muscular coat is developed in very various degrees, & with different kinds & intensities of mechanical stimuli, I have never yet been able

to detect the slightest wave of contraction moving away from the point stimulated to the other parts of the artery. Notwithstanding this, such observations as the above show how extremely sensitive to slight mechanical stimuli is plain muscular tissue and, as one variety of it, arterial muscle. If we should wish to explain arterial tonicity, however, as due to any mechanical stimulus, we should be obliged, owing to the non-peristaltic character of the arterial contraction, to suppose such a stimulus to act at all points along the course of a vessel. Now it seems to me that we have in the shock given to the arteries by the beat of the heart all the requisites of a tone-

producing stimulus applied to the arterial muscles. The shock given to the larger arteries by each heart beat is considerable as is indicated by the distinctness with which the pulse is felt by a finger; & even in the microscopic arterioles the blood can be seen to move intermittently. It seems not improbable that the mechanical stimulus is sufficient to slightly affect the muscle cells. The resulting contraction would not have time to run its full course & disappear before a second stimulus would come in the shape of a second pulse wave and a second contraction would be fused with the first. Moreover the same phenomena would appear practically simultan-

sively at every point throughout the whole arterial system & the result would necessarily be a tonic constriction of all the arteries.

I have continued the experimental investigation of this theory, begun by Stevens & myself. My apparatus was arranged as in the above experiments upon the action of drugs. The experiment was however usually begun with a constant inflow and this was kept up until the outflow & pressure were each fairly regular & uniform. The heart was then set to work, making the inflow a rhythmically interrupted one and the effects upon the pressure & the outflow were noted. But here at once arose a difficulty which I have thus far been unable to

overcome; by the beat of the heart the inflow is made greater than during constant pressure since the liquid is pumped into the arteries with a considerable force & not simply allowed to run in by force of gravity. At the same time the pumping in of a greater quantity of liquid increases the pressure within the arteries. This increase in flow & increased pressure has an augmenting effect upon the outflow & seriously complicates matters as regards the recognition of a slight constriction or dilation, which the heart beat may cause. In cases where the vasomotor effect is sufficiently great the difficulty is of less importance, as indicated by the following statistics taken from

Experiment 17, Feb. 4, 1885.

Time P.M.	Temperature of Circulating fluid in C	Arterial Pressure in mm Hg	Venous Outflow per minute in cc	Remarks
4.20	28	15.	1.7	Constant Inflow
.23	27.8	13	2.1	
.26	28.1	15.2	2.2	Heart started at 30 beats
.27		16.7		per minute
.29	28.1	16.5	2.2	
.32	28.	16.8	1.7	
.35	27.5	17.7	1.6	
38	27.	18.1	1.4	
.41	26.7	17.8	1.2	
.44	28.2	17.6	1.2	
47	27.	17.3	1.5	Heart stopped
.51	26.6	15.2	1.4	Constant Inflow
.54	26.1	15.2	1.2	
.57	26.	15.2	1.1	
5.00	25.8	15.2	0.9	
.03	25.3	15.2	0.8	

5.06	27.7	15.2	7	
09	30.	15.2	7	
12	28.9	15.2	.5	
.15	29.3	15.2	.6	
18	30	15.2	.5	
21	28.1	15.2	.6	
24	28.4	15.2	.8	
27	30	15.2	.8	
30	30.2	15.2	1	
33	29.	15.2	1.	
36	29	15.2	1	
.39	30.	15.2	1.1	
42	30.	15.2	1.	

Here the first result of the heart's action is to throw into the arteries in a given time a larger quantity of blood than has been going on by constant flow. We

should^thus^ expect a rise of pressure at first due to the presence of this increased quantity of fluid, & we see such a rise at 4.27, one minute after the heart was started. The extra liquid quickly diffuses itself throughout the whole arterial system & the pressure falls to 16.5 m.m. But the slowly appearing tonic contraction begins to manifest itself & the pressure rises to a higher level than at first, while at the same time the outflow gradually diminishes, notwithstanding the fact that the tendency of the heart beat is to maintain a larger inflow. After the stoppage of the heart a curious phenomenon is observed which was noticed

ed by Stevens & myself. The outflow gradually diminishes sometimes to almost complete stopping, then slowly increases to a constant, which is however usually lower than that during the intermittent inflow. This gradual diminution of outflow may be explained by supposing the tonic contraction caused by the heart tends to continue after the stimulus is removed, just as with the slight stimulus of the pinch of the forceps the resulting contraction rises to and remains at its maximum for some time before giving place to relaxation. The persisting contraction is now able to manifest itself in a greatly decreased outflow, the

latter not being masked as it is when the heart is beating.

From the above considerations it is evident that undoubted constriction of the arteries may be caused, the only stimulus to which is the shock of the heart beat. Such constriction is slow to appear & is extremely persistent. Any theory of the cause of arterial tonicity would be incomplete, however, did it not offer an explanation of dilation as well as of constriction. If we suppose the normal beat of the heart to produce normal tonicity of the arteries, we naturally look to variations in the normal beat for the explanation of variations in the

degree of such tonicity. Variations in the heart beat may be of two kinds — those in rate + those in power. If we attempt to introduce variations of this character into our experiments with the artificial heart we introduce a similar difficulty ~~to~~ that above mentioned - altering the rate or power of beat mechanically alters at the same time the inflow + the arterial pressure. Overlooking this trouble, however, I have made many careful experiments, testing the effect of changes in the character of the heart beat but have not obtained results sufficiently harmonious to justify the deduction of a general law bearing upon the question of arter-

ial dilation. Sometimes with an increased rate or increased power of beat, an apparent constriction took place, sometimes an apparent dilation. So far then as I am able to say at present the question of variations in arterial tonicity depends in no wise upon the question whether the heart beats more or less rapidly or more or less forcibly. Further experimentation is, however, needed to absolutely determine this. Failing to obtain undoubted dilation by these methods, I sought it in another way & obtained more satisfactory results.

In investigating the mode of action of vasomotor nerves,

Lépine (5) found that if a dog's foot were plunged into cold water & the arteries thus constricted by the low temperature, then a stimulus applied to the nerve supplying the foot would cause dilation; & vice versa, if the arteries had been previously dilated by heat, a stimulus of the same nature as before would produce constriction. He hence concludes that the whole question of vasomotor constriction or dilation depends upon the condition of the arteries at the moment of stimulation; if this condition is one of constriction, stimulation gives dilation; if dilation exists, the ac-

tion of the nerves to cause constriction. The possibility of thus obtaining dilation has been confirmed by Bernstein (6) & I have applied the same principle in my own investigation. In order to first constrict the vessels, I have found the best method to be by cooling the fluid which is to be circulated. A constant inflow is employed until the constriction manifests itself in a diminished outflow. The heart is then set to work while the circulating fluid is still kept cold. The first effect is the momentary rise of pressure due to the increased quantity of liquid

entering the vessels. Then follows a steady fall of pressure accompanied by a greatly increased outflow. After the cessation of the stimulus the outflow again diminishes. For the details of a typical case see the following table, taken from Experiment 13, Jan. 27, 1885.

Time P.M.	Temperature of Circulating Fluid, C	Arterial Pressure in mm Hg	Venous Outflow in CC per minute	Remarks.
4.09	18.2	14.4	1.7	Constant inflow
.12	18.1	14.4	1.9	
.15	18.9	15.2	.7	
.18	19.2	14.4	.5	Heart started
.19		19.9		
.21	14.	17.9	3.	
.24	13.	16.3	8.3	
.27	12.5	15.9	11.1	

4.30	12.3	15.9	11.3	
.33	13.5	15.7	10.1	
36	12.6	17	9.6	
.39	13.2	21.4	7.5	Pressure becoming very ir-
.40		17.2		regular
42	13.3	26.	7.6	
45	13.3	18.1	6.5	Heart stopped.
48	15	14.2	4.5	
51	16.	14.4	1.3	
54	16.8	14.3	6	
.57	17.	14.3	.6	

The increased outflow ~~[illegible]~~ accompanying the hearts' action was from 0.5 cc. to 11.3 cc while the fall in pressure was from 19.9 mm to 15.9 mm. & then to 15.7 mm. At 4.39 for some unaccountable reason the pulse tracing became irregular, rising & falling

alternately + the heart was then stopped.

Now it seems hardly reasonable to suppose that this great increase in outflow resulting from the action of the heart was due to the increased quantity of liquid pumped into the arteries. But to guard against an objection of this kind it was thought best to determine by actual experiment the mechanical effect of the heart beat upon the outflow by means of an artificial schema. For this purpose the terrapin's body was removed from the box, in which it lay during the experiment, the inflow tubing coming from the artificial heart was joined directly to the outflow tubing + an endeavor was

made by partially clamping the latter, to fix the outflow per minute at 0.5 cc, which was the outflow from the animal at 4.15. After several trials the flow became constant at 0.6 cc. while the pressure stood at 14.2 m.m. and the heart was then started with the same rate & force as at 4.18. But the outflow was thereby increased to only 2.5 cc + would not go above this, although, owing to the great elasticity of the rubber tubing, the pressure rose to 91.7 m.m. The great difference between 2.5 c.c., the outflow obtained from the schema, + 11.3 cc., the outflow produced when the animals arteries were in the circulation, is then only to

be explained upon the theory of an active dilation of the arteries. It is noticeable too that in the above experiment during the action of the heart, the temperature of the circulating liquid fell several degrees, thus interposing a powerful obstacle to the dilation & doubtless modifying its intensity. Results similar to the above have been obtained in many cases.

Dilation has been several times obtained when the arteries have not been previously constricted, either by cold or by any other artificial means, &, on the other hand, constriction has resulted, when the arteries have not been previously dilated by the circulation of

warm liquid. (For an example of constriction after such dilation see Experiment 17, p.38). The want of harmony in the results has hence up to the present prevented me from being able to say under exactly what conditions the choice of actions is made by the arteries. Active dilation is always obtained when the arteries are previously constricted by cold. On the contrary active constriction is not so easily obtainable after previous heat dilation. The overcoming of the above mentioned difficulties & the employment of more delicate means of experimentation & observation might show fewer apparent exceptions to

the theory of Lépine + Bernstein. My results so far argue for its probable applicability to the case of arterial tonicity as maintained by cardiac action. Were it the correct explanation, we cannot understand how the beat of the heart might cause simultaneously dilation in one vascular area + constriction in another.

It seems then that we may look to two different agents in seeking the cause of the maintenance of arterial tonicity, viz. the alkaline salts of the circulating liquids + the beat of the heart. In the first case the tonicity may be set aside by heat generated by protoplasmic activity; in the second case it seems prob

able that the condition of the vessels themselves determines when dilation shall appear. In either case the character of the stimulus does not require the intervention of nerve cells, and, until the existence of such elements as a constant factor in the tissues of the arterial walls is proven, we are justified in assuming tonicity to be a purely muscular phenomenon.

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